quate drainage of the bile reduces this hypercholesterinemia, and that these patients, if promptly put upon properly selected diet, will not develop a hypercholesterinemia. Whether or not they may develop subsequent symptoms we must at present leave open until we have observed our cases for a longer period of time. However, we feel that if the hypercholesterinemia can be controlled we will have solved at least one of the important etiological factors in these individuals suffering from chronic cholelithiasis.

INFLUENZAL MENINGITIS, WITH REPORT OF A CASE.[1]

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Cerebrospinal meningitis caused by the influenzal bacillus is reported not infrequently, and probably often occurs without recognition, as there is nothing in the course or symptomatology of this disease to distinguish it from meningitis due to other acute infections. The only means of diagnosis is a careful bacteriological examination of the spinal fluid.

In 1911 Flexner[2] published a summary of the information possessed regarding this condition up to that date, and earlier in the same year Wollstein[3] reviewed this subject thoroughly, collecting 49 cases from which the influenza bacillus was recovered in pure culture and 9 in which it occurred with other organisms. Simon,[4] at about the same time, reported 2 cases and collected 41, including 12 not in Wollstein's series. These two series combined gave a total of 61 cases of pure infection and 9 of mixed, with only five recoveries. Since that time I have noted reports of 26 additional cases with two recoveries. A review of these reports tends to confirm previous figures regarding the high mortality of the disease. Including my own case, 89 cases show only eight recoveries.

Wollstein seems to have made a real advance in the specific treatment of this infection. A serum was prepared by immunizing a goat by means of virulent strains of the influenza bacillus, and with this serum she was able to successfully control experimental influenzal meningitis in monkeys.[5] The disease was rapidly and invariably fatal in the untreated animals, but complete recovery without complications was obtained by the intra-dural injection of serum.

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[1] Read before the Section on Internal Medicine of the College of Physicians of Philadelphia, January, 1916.

[2] Jour. Am. Med. Assn., vii, No. 1, 16.

[3] Am. Jour. Dis. of Children, 1911, 1, 42.

[4] Monatschrifte f. Kinderheilk., 1910, 9, 549, orig.

[5] Wollstein, Jour. Exp. Med., 1911, xiv, 73.

The case reports published since Wollstein's paper appeared include the following:

1. Hymanson. *New York Med. Jour.*, December 5, 1909. Age, six and a half months. Fatal. Ill three weeks.
2. Age, eight months. Fatal. Ill ten days.
3. Brem and Zeiler. *Am. Jour. Dis. of Children.* 1911, I, 417. Age, eighteen months. Fatal.
4. Age, twenty-three months. Fatal.
5. Clemens and Gould. *Arch. Ped.*, 1911. Age, seven months. Fatal. Ill eight days.
6. Rhea. *Arch. Int. Med.*, 1911, viii, 132. Age, six months. Fatal. Ill four days.
7. Age, five years. Fatal. Ill eighty-nine days. (Internal hydrocephalus.)
8. Klinger. *Correspond.-Blatt. f. Schweiz. Aertz.*, 1912, 1289. Age, two years. Fatal.
9. Age, five years. Fatal.
10. Age, five years. Fatal.
11. Age, twenty-six years. Recovery.
12. Jündell. *Hygiea,* Stockholm, 1912, lxxiv, No. 3. Infant. Fatal.
13. Giese. *Ugesk. f. Laeger.*, 1913, xxv. Ref. *Jour. Am. Med. Assn.*, 1913, 1, 1675.
14. Ross and Moore. *Brit. Med. Jour.*, 1913, II, vol. 25. Age, thirteen months. Fatal. Five punctures.
15. Tebbut. *Med. Jour. Australia,* October 31, 1914. Age, eight months. Fatal. Ill thirteen days.
16. Grasty. *Am. Jour. Obst.*, lxvii, 1031. Age, two years. Fatal. Ill fifteen days.
17. Ely and Weingart. *Jour. Iowa State Med. Soc.*, 1915, v-x. Age, three and a half years. Fatal. Ill eighteen days.
18. Hill and Packard. *Lancet-Clinic,* 1915, xii, 723. Age, twenty-two years. Fatal. Ill sixteen days.
19. Age, two years. Fatal. Ill two weeks.
20. Age, five months. Fatal. Ill nineteen days.
21. Age, four months. Recovery. Ill thirteen days.
22. Age, five months. Fatal. Ill seven days.
23. Prasek and Zatelli. *Wien. klin. Wchnschr.*, xxiv, No. 26. Age, eighteen months. Fatal. Ill sixteen days.
24. Boland. *Lancet,* 1915, II, 704. Age, four months. Fatal. Ill fifteen days.
25. Ducrot. *Rev. méd. de la Franche comté.* Age thirty-two years. Fatal. Ill six days.
26. Imperatori. *Laryngoscope,* 1915, 580. Fatal. Ill twelve days.
27. Torrey. Age, eleven years. Recovery. Ill four weeks.
28. Age, eight months. Fatal. Ill seventeen days.

Herbert Henry[6] reports 9 cases of meningitis in which an influenza-like organism was recovered from the spinal fluid. In three of these cases the fluid was sent to his laboratory for examination, but he did not get reports on the clinical history of the patients. In 2 the culture died without sufficient study. Henry regards the organism as similar to, but distinct from, the true Pfeiffer bacillus, though from the description of the cultures and inoculation experiments it seems probable that he was dealing with the influenza bacillus.

Sayce[7] reports 7 similar cases of meningitis occurring in Melbourne from 1906 to 1910. One patient lived for six months; in all the others the duration of disease was under three weeks. The ages varied from five months to five years. One patient, aged four years, recovered; all the others died. Sayce was unable to say whether this organism was identical with the influenza bacillus, but, as in Henry's cases, the description makes it seem probable that these were cases of influenzal meningitis. Owing to the doubt expressed as to the identity of the organisms, these cases are not included in the above series.

My case was of particular interest in that it afforded an opportunity for the trial of Wollstein's serum, of which a supply was furnished through the kindness of the Rockefeller Institute.

Case I.—A girl, aged eleven years, of good development, in normal health, intelligent and bright, became ill on November 15, 1915. Showed fever, general muscular pains, chills, stuffy feeling in the head, and vomiting. She complained of a very severe headache localized over the left eye, and occasional nausea and vomiting. She showed a pulse of 120 and a temperature of 103°. Marked tenderness over the frontal sinus on the left. Lungs were normal. Reflexes normal. No stiffness of the neck.

November 16. Examined by Dr. Packard, who reported that he found the nose and ears normal, and could find no evidence of any pus collection in the sinuses. Tenderness over the sinus has now disappeared.

November 17. Seen by Dr. Stengel in consultation. There was stiffness of the legs and pain down the legs and marked rigidity of the neck. Kernig's sign present. Photophobia marked. Temperature continued from 102° to 104°. Mentality clear. Knee-jerks diminished. Spinal puncture showed fluid turbid and under increased pressure. The smear from this fluid showed the turbidity to be due to cells which were nearly all polymononuclear, and there were present great numbers of organisms both in the cells and free. Dr. Wolferth, who examined the specimen, stated that the organisms seen on the smear were probably meningococci, but that they were not typical, and that he could not make a certain diagnosis until he had cultered the fluid. About 30 to 40 c.c. of fluid was withdrawn and 15 c.c. of antimeningococcic serum introduced. There was a drop of temperature and marked relief from the subjective symptoms following the tapping, but the temperature rose again after a few hours. The stiffness of the neck increased and retraction of the head and arching of the back became very marked. The patient is now lying on the side with the head stiffly retracted, so that the back of the head lies almost against the spinal column. There is no paralysis of the arms, but movement of the legs caused a great deal of pain.

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[6] Jour. Path. and Bact., xvii. 174.

[7] Australian Med. Jour., 1911, xvi, 25.

November 18. The second injection of antimeningococcic serum was given today. The fluid was more turbid than at the first tapping, but the organisms were found to be largely intracellular. Hexamethylenamin, gr. x, every six hours.

November 20. Dr. Wolferth reported a pure culture of influenza bacillus, and a supply of anti-influenza serum was kindly forwarded from the Rockefeller Institute. There was very marked retraction of the head and stiffness of the back, and slight internal strabismus of the right eye. Diminished knee-jerks. Temperature from 102° to 104°. Pulse 108 to 120. Mentality clear. Considerable twitching, also hoarseness and great difficulty in swallowing. Thirty c.c. of fluid were withdrawn. Very turbid, organisms practically all intracellular. Fifteen c.c. of the serum introduced. There was very intense pain in the hip, thigh, and leg on the side which the patient lay. This seemed to be accompanied by muscular spasm, and was apparently agonizing in its intensity. After introducing the serum there was, as before, a prompt subsidence of the temperature and pulse, followed by a sharp febrile reaction which lasted a few hours and dropped again. The condition of the patient now seemed better than before, and the back was a little less rigid, the strabismus disappeared, photophobia less. Seen by Dr. Martin in consultation.

November 21. Less arching of the back, the neck retracted as before, considerable difficulty in swallowing, and some hoarseness. Patient seemed brighter than the day before. Slept at short intervals. Injected 15 c.c. anti-influenzal serum, after withdrawal of 35 c.c. very turbid fluid.

November 23. Lumbar puncture. Removal of 30 c.c. Very turbid. Injection of 15 c.c. of anti-influenzal serum. This injection caused extreme pain in the legs, as did the previous ones. Occasionally slightly delirious.

November 28. Temperature has ranged from 99° to 103.4°, with irregular course. The pulse, for the most part, below 100, and the patient, on the whole, has seemed very much better for the past few days. Sleeping well all night. Mentality clear. Spinal puncture was done today and 40 c.c. of fluid withdrawn.

December 1. Very irritable; exceedingly hungry all day. Neck more mobile, no pain. Pupils show prompt reaction, no strabismus.

Knee-jerks normal. Spinal fluid opalescent, less turbid than previous specimen, and fair amount of fibrin collected on standing. Organisms somewhat fewer yesterday, all intracellular. Pressure, 300 mm. Withdrawal of 35 c.c. fluid. Vertical and temporal headache, which quickly subsided. Pressure 180 mm. Patient looks much better than heretofore. Less irritable, and less nervous after tapping.

December 2. Temperature has been normal all the afternoon. Pulse regular; 88 to 96. Pressure, 300 mm. Took out 7 c.c. more after brief rest. Back less rigid, appetite good, still somewhat irritable, no pain. Spinal fluid shows slight opalescence; about the same as yesterday. Six rabbits injected day before yesterday, two controls with emulsion of bacilli, four animals with serum and emulsion. All are alive and apparently well.

December 3. Thirty-five c.c. withdrawn, pressure dropped from 28 to 14 cm. With the withdrawing of the final 5 c.c. pressure fell to 11 cm. The smears from this fluid showed few organisms, and they were contained in relatively few cells, *i. e.*, an occasional leukocyte was found which was full of organisms, but these were rare.

December 4. Withdrew about 35 c.c., slightly turbid. Smear showed no organisms. Pressure 26 cm., fell to 14.

December 5. Temperature normal; pulse 100 to 108; no tapping. No pain or headaches.

December 6. Temperature reached 102° last night; pulse 112. Slept soundly, but there was a good deal of twitching of the muscles during sleep. Today, seems very well, appetite good, pulse perfectly regular, no pain, neck still retracted. Did not tap.

December 17. Another puncture was done on December 8 on account of nervousness and irritability. Pressure was 26 cm., which was reduced to 13 cm. by withdrawal of 30 c.c. of fluid. Fluid showed very slight turbidity. No organisms found in the smear. Leukocytes and polynuclears about equal in number. Thereafter the temperature remained about normal, never reaching 99. On December 15 another puncture was done. Thirty c.c. of clear fluid withdrawn. The pressure fell from 17 to 8 cm. Fluid perfectly normal in appearance. Both of the specimens were negative to culture. All the previous ones were cultured and showed the influenza bacillus alone. After the last puncture there was a prompt clearing up of the nervousness and irritability.

SUMMARY. This patient apparently had a severe attack of influenza with a frontal sinus infection, followed by typical cerebrospinal meningitis. The organism isolated from the case showed a low degree of pathogenicity when tested by injection into rabbits. The spine was tapped thirteen times, and the influenzal organism present up to the last two tappings. There was an improvement of the symptoms following each tapping, both when the serum was used and when it was not employed. The fluid was more turbid following the first injection of antimeningococcic serum. It remained turbid as the organisms became fewer. The organisms at first were to a certain extent extracellular, but after the first injection of serum, they were almost always within the cells. The temperature was irregular throughout, but it was noted that following each tapping or injection there was a rise in temperature for a few hours. The use of the influenza serum was discontinued because the patient seemed to be improving, and because of the pain occasioned by its injection. With the clearing up of the organisms in the fluid, the temperature remained at normal, and the stiffness of the neck, which was the last remaining symptom, gradually disappeared.

Recovery was apparently complete with no nervous symptoms remaining. The only signs of high-pressure noted were extreme restlessness and irritability, which cleared up promptly with the removal of from 25 to 40 c.c. of fluid.

Case II.—M. G., American; aged eight months. Admitted to University Hospital October 28, 1914. Service of Dr. Frazier. Referred to Dr. Griffith's service. Through their courtesy I am permitted to report this case.

History of stiffness of neck, lump on head, refusal to eat, and vomiting. Has had a cold since August, but was bright and active until two weeks ago. Since then he has been very quiet and has not taken his feedings well; cough has become worse, neck has been stiff, and he has been feverish. Two weeks ago the mother noticed lump on his head, and for two weeks he has had attacks of vomiting.

Examination shows fair development, pallor, opisthotonos, no tâche, marked bulging of anterior fontanelle, irregularity of pupils, neck very rigid. Chest shows harsh breath sounds at both apices and moist rales all over lungs. Breathing of Cheyne-Stokes type. Heart action regular, abdomen negative. Kernig's sign positive.

After lumbar punctures there was less bulging of the fontanelle. Puncture yielded turbid fluid under increased pressure.

Dr. Wolferth reported numerous bacilli free in the fluid with practically no phagocytosis. These cultures were thoroughly studied and afterward reported as influenzal bacillus of the meningeal type in pure culture.

This patient lived for three days after admission to the hospital. He had frequent convulsions and attacks of vomiting and was stuporous throughout. The temperature varied from 102° to 105°, the pulse from 130 to 165, and the respiration from 36 to 45. The treatment included stimulation, hot packs and baths, and urotropin.

A summary of the literature on influenzal meningitis shows that this disease is not rare, that it has an extremely high mortality rate, that the majority of cases occur in infants or young children, and that the death rate is higher in the young; that it cannot be distinguished from other forms of meningitis except by bacteriological examination of the cerebrospinal fluid; that the bacilli pass freely from the cerebrospinal space to the general circulation and cause a general bacteremia, and that secondary infections in the various organs are common.

The following recoveries are reported:

1. Langer. *Jahrb. Kinderheilk.*, 1903–91. Age, nine years. Ill twenty-seven days. (Recommends lumbar puncture.)
2. Caccia. *Monat. f. Kinderheilk.*, 1903–41. (Mya.) *Gaz. degli Osped.*, 1903, XXVI, 269. Age, nine months. Ill forty-two days. (Believe recovery the result of repeated lumbar puncture.)
3. Thomesco and Grascaski. *Rev. Neurologique*, 1904. Age, seven years. Ill ten days.
4. Cohoe. AM. JOUR. MED. SC., 1901, cxxxvii, 74. Age, thirty-three years. Ill thirty-four days.
5. Batten. *Lancet*, 1910, 1677. Age, fourteen months. Ill seventeen days.
6. Hill and Packard. *Lancet-Clinic*, June 26, 1915. Age, four months. Ill thirteen days. (Note marked improvement in condition following lumbar punctures.)
7. Klinger. 1912. Age, twenty-six years. Injection of electrargol (intravenous), daily for one week.

A personal communication from Dr. Packard of Philadelphia tells me of a case in which there was an infection of the middle ear and mastoid of a child. Symptoms of spinal meningitis prompted lumbar puncture, and a turbid fluid, under high pressure, was obtained which yielded influenza bacilli in pure culture. The symptoms cleared up, and the fluid became clear after four injections of influenza serum furnished by the Rockefeller Institute. This patient later had a complication of a brain abscess, with infection of a different type, which also ended in recovery.

This case will later be reported in detail.

Regarding treatment, there are three measures recommended which deserve serious consideration.

1. The anti-influenzal serum of Wollstein, whose action appears to be specific. Where practical, this serum should certainly be tried.
2. Hexamethylenamin, which has been recommended by a number of writers, notably Brem and Zeiler, and by Batten. The latter reports a case in which recovery followed its use. There seems, however, to be less basis for regarding it of great value than is the case with either Wollstein's serum or repeated spinal puncture and drainage.
3. Repeated lumbar puncture.

Drainage of the subarachnoid space by means of lumbar puncture has been practised extensively since it was first proposed by Quincke. Many writers make the assertion that in meningitis this procedure may relieve pressure symptoms, but can have no curative effect. In view of the reports of severe cases of meningitis, even of the pneumococcic and tuberculous varieties, showing recovery following repeated lumbar puncture, these statements seem unwarranted. There is an immediate and very striking temporary good effect, probably due directly to the relief of excessive intracranial tension and improved blood supply in the tissues of the brain and cord. There is also removal of the toxins which would otherwise be absorbed into the circulation. Improvement in the circulatory conditions following decreased pressure may have an effect in combating local infection. It is believed that under normal conditions the cells of the choroid plexus, in secreting the cerebrospinal fluid, act as an effective barrier to most toxins and antibodies. It has not, as far as I know, been demonstrated that antibodies do not pass into the spinal fluid in cases of meningitis where there is an active inflammation of the membranes, and leukocytes pour into the fluid in enormous numbers, and the conditions are far from normal. The increased phagocytosis and decrease in organisms which has been demonstrated following lumbar puncture suggest that with the resulting lowered pressure, and increased outpouring of fluid into the cerebrospinal space, protective substances may pass from the circulation into the spinal fluid.

A further benefit probably derived from frequent spinal drainage is protection in part against the development of that much feared complication of meningitis—internal hydrocephalus—as the rapid flow of fluid from the ventricles tends to keep the foremen of Majendie clear of exudate which might cause obstruction at this point.

In my case there appeared to be temporary improvement following the use of antimeniningococcic serum, which was employed before the culture reports showed the nature of the infection. This, of course, may have been partially due to the removal of spinal fluid, or to the effect of the serum, or independent of either. Following the use of anti-influenzal serum, the improvement was very striking for two days. Simple lumbar puncture and drainage was substituted for the serum treatment on account of the severity of the pain following the introduction of the serum. Had improvement not been satisfactory under this procedure, serum would have again been used, possibly with a previous introduction of novocain.

The spinal fluid was withdrawn slowly until marked discomfort was caused by temporal headache. The pressure was measured by a glass tube of small caliber connected with the needle. It was noted that at each tapping the pressure could be reduced about one-half before uncomfortable symptoms developed.

A review of the cases which have recovered seems to emphasize the value of lumbar puncture as a therapeutic measure in meningitis, and experimental results indicate that the anti-influenzal serum there is available a specific agent which should be employed in meningitis due to the influenza bacillus.